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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,554	12/17/2001	Thomas Maciag	54474-5005	3856

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 09/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,554	MACIAG ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *18-26 and 28-48* is/are withdrawn from consideration.

5)☒ Claim(s) *1-17* is/are allowed.

6)☒ Claim(s) *27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/12/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 6/30/04. Claims 1-48 are currently pending in the application and are addressed herein.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-17 and 27) in the reply filed on 6/30/04 is acknowledged.

Claims 18-26 and 28-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/30/04.

Claims 1-17 and 27 are examined herein.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. For example, see page 18 of the specification. Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are drawn to an isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin degradation, wherein said nucleic acid encodes a polypeptide wherein the amino acid residue at position number 136 in SEQ ID NO:2 is lysine (claim 7); and an isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin degradation, wherein said nucleic acid encodes a polypeptide wherein the amino acid residue at position number 136 in SEQ ID NO:2 is not arginine (claim 8).

A careful analysis of the claim reveals that the claims do not explicitly indicate that the isolated nucleic acids encode the polypeptide that is SEQ ID NO:2 with the exception that lysine is present at position 136 of SEQ ID NO:2, or with the exception that arginine is not present at position 136 of SEQ ID NO:2. As such, the claims can be interpreted as being drawn to a nucleic acid encoding an fibroblast growth factor-1 (FGF-1) resistant to thrombin degradation wherein the sequence of said FGF-1 could be completely different from the amino acid sequence set forth in SEQ ID NO: 2, yet contain a lysine residue at position 136 of SEQ ID NO: 2 (or not contain an arginine at position 136 of SEQ ID NO:2). Therefore that instant claims are indefinite because it is unclear how an FGF-1 that is resistant to thrombin and that is completely different from SEQ ID NO:2 could comprise a lysine at position 136 of SEQ ID NO:2, (or could not contain an arginine at position 136 of SEQ ID NO:2) when the claim does not explicitly indicate that the FGF-1 comprises SEQ ID NO:2.

It is pointed out that amending the claims to read:

An isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin degradation wherein said nucleic acid encodes the amino acid sequence of SEQ ID NO:2 with the exception that a lysine is present at amino acid position number 136 of SEQ ID NO: 2; and

An isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin degradation wherein said nucleic acid encodes the amino acid sequence of SEQ ID NO:2 with the exception that a arginine is not present at amino acid position number 136 of SEQ ID NO: 2; would obviate the rejection of claims 7 and 8.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between

function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

The instant claim is drawn to a composition comprising an isolated nucleic acid encoding a FGF-1 resistant to thrombin degradation, wherein the nucleic acid comprises the sequence of SEQ ID NO: 3, or fragment, or derivative thereof, and a pharmaceutically acceptable carrier.

Therefore, the claims encompass a genus of nucleic acid molecules that are derivatives or fragments of SEQ ID NO: 3 that encode a FGF-1 resistant to thrombin degradation. As such, the genus of nucleic acid molecules encompasses an incredibly large number of different species molecules considering all possible derivatives and fragments of SEQ ID NO: 3 that could encode a thrombin resistant FGF-1 fragment or derivative, including molecules that have yet to be discovered.

The specification has disclosed the thrombin degrades wt FGF-1; however, the mutant FGF-1 protein (encoded by SEQ ID NO: 3) is resistant to thrombin degradation. Applicants have thus discovered that the arginine residue at position 136 of FGF-1 polypeptide is critical for thrombin degradation. Applicants have shown the critical importance of the arginine at position 136 by mutating the arginine to lysine at position 136 of FGF-1 (i.e. FGF-1_{R136K}).

Applicants have not, however, described a "representative number" of species encompassed by the claims. In order to determine if a representative number of species have been described, one has to take into account the number of species encompassed by the claims. Since the claims encompass all derivatives and fragments of FGF-1 that maintain FGF activity but are resistant to thrombin degradation, the claims encompass a incredibly large number of possible variants of SEQ ID NO: 3, including variants that have not been described in the

specification. Furthermore, since applicants have not disclosed the minimal sequence of FGF-1 that is critical for FGF-1 activity, such as by describing the required functional domains of FGF-1, then one of skill in the art would not recognize which derivatives/variants of FGF-1 (other than the amino acid 136 point mutation) would have FGF-1 activity and be resistant to thrombin degradation. That is, no structure-function relationship of FGF-1 has been adequately described such that one of skill in the art would be able to recognize the FGF-1 derivatives/variants encompassed by the claims without performing additional experimentation.

Additionally, claim 27 is also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, in view of the written description rejection above. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As mentioned above, the claims encompass molecules for which there is insufficient written description provided in the specification, and include variants, fragments and derivatives of disclosed sequences. Without a clear written description of the molecules encompassed by the claims one of skill in the art would not know how to make and use the claimed invention without performing an undue amount of additional experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by Shireman et al. (Journal of Vascular Surgery, Feb. 2000).

The instant claim is drawn to a composition comprising an isolated nucleic acid encoding an FGF-1 resistant to thrombin degradation, wherein the nucleic acid comprises the sequence of SEQ ID NO:3, or a fragment, or derivative thereof, and a pharmaceutically acceptable carrier. It is pointed out the phrase "derivative thereof" renders the claim very broad, as the term is not specifically defined in the specification. Given the broadest reasonable interpretation a "derivative" of SEQ ID NO:3 would include any FGF-1 polypeptide that was resistant to thrombin degradation.

Shireman teaches a nucleic acid that encodes an FGF-1 that is resistant to thrombin degradation. Specifically, Shireman teaches the creation of a nucleic acid encoding an FGF-1 resistant to thrombin degradation by utilizing site directed mutagenesis to make an S130K substitution in the FGF-1 polypeptide. Shireman teaches that PCR was used to create the mutation in the nucleic acid and that the plasmid containing the mutation was purified from individual bacterial colonies (e.g., see 384, first column). The purification of the plasmid comprising the mutant nucleic acid would necessarily encompass a composition comprising the plasmid in a pharmaceutically acceptable carrier. As such, Shireman teaches all of the limitations of the claim and thus anticipates claim 27.

It is noted that limiting the claim to a composition comprising an isolated nucleic acid encoding an FGF-1 polypeptide that is resistant to thrombin degradation and wherein the nucleic

acid comprises the sequence of SEQ ID NO: 3 and a pharmaceutically acceptable carrier would obviate this rejection.

Allowable Subject Matter

Claims 1-6 and 9-17 are allowed.

It is also pointed out that amending claims 7 and 8 to specifically recite that the isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin degradation wherein said nucleic acid encodes the amino acid sequence of SEQ ID NO:2 with a lysine present at amino acid position number 136 (for claim 7) and wherein the amino acid at position 136 is not arginine (for claim 8) would obviate the rejection of claims 7 and 8. Furthermore, amending claim 27 to: a composition comprising: 1) an isolated nucleic acid encoding a FGF-1 resistant to thrombin degradation, wherein the nucleic acid comprises the sequence of SEQ ID NO: 3, and 2) a pharmaceutically acceptable carrier; would obviate the rejection to claim 27.

Conclusion

Claims 1-6 and 9-17 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art unit 1635

DAVE T. NGUYEN
PRIMARY EXAMINER